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<110> Tosoh Corporation

<120> IL-6 RECEPTOR IL-6 DIRECT FUSION PROTEIN

<130> Q62375

<140> 09/743,239
<141> 2001-01-05

<150> JP Hei. No. 10-190597
<151> 1998-07-06

<150> JP Hei. No. 11-21788
<151> 1999-01-29

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<151> 1999-04-30

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aatattatca tcgtctttat tagtagtaag t 91

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<212> DNA
<213> Artificial Sequence

<220>
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<212> DNA
<213> Artificial Sequence

<220>
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cggggcttta ttagtagtaa gt 22

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acttactgcc ccggtac 17

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<400> 40
cggggcagta agt 13

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<212> DNA
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<220>
<223> Primer

<400> 46
agatctggat tctgtccaag gcgtgcccat ggc 33

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<220>
<223> Primer

<400> 47
agatctggta cccccaggag aagattcc 28

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<400> 50
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<210> 51
<211> 33
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<400> 51
ctcgagaaga gggttccccc cgaggagccc cag 33

<210> 52
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<212> DNA
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<223> Primer

<400> 52
tctctagaga atattatcat cg 22

<210> 53
<211> 29
<212> DNA
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<223> Primer

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ctcgagaaga gggagcccca gctctcctg 29

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<400> 54
tctctagaga atattatcat cg 22

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tctcgcgatg tagccgcccc acac 24

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<400> 56
atgcggccgc tacatttgcc gaagagccc 29

<210> 57
<211> 33
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<400> 61

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1 5 10 15

<210> 62
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<213> Artificial Sequence

<220>
<223> Linker

<400> 62

Ser Ser Glu Leu Val
1 5

<210> 63
<211> 468
<212> PRT
<213> Homo sapiens

<400> 63

Met Leu Ala Val Gly Cys Ala Leu Leu Ala Ala Leu Leu Ala Ala Pro
1 5 10 15

Gly Ala Ala Leu Ala Pro Arg Arg Cys Pro Ala Gln Glu Val Ala Arg
20 25 30

Gly Val Leu Thr Ser Leu Pro Gly Asp Ser Val Thr Leu Thr Cys Pro
35 40 45

Gly Val Glu Pro Glu Asp Asn Ala Thr Val His Trp Val Leu Arg Lys
50 55 60

Pro Ala Ala Gly Ser His Pro Ser Arg Trp Ala Gly Met Gly Arg Arg
65 70 75 80

Leu Leu Leu Arg Ser Val Gln Leu His Asp Ser Gly Asn Tyr Ser Cys
85 90 95

Tyr Arg Ala Gly Arg Pro Ala Gly Thr Val His Leu Leu Val Asp Val
100 105 110

```
Pro Pro Glu Glu Pro Gln Leu Ser Cys Phe Arg Lys Ser Pro Leu Ser
        115                 120                 125

Asn Val Val Cys Glu Trp Gly Pro Arg Ser Thr Pro Ser Leu Thr Thr
    130                 135                 140

Lys Ala Val Leu Leu Val Arg Lys Phe Gln Asn Ser Pro Ala Glu Asp
145                 150                 155                 160

Phe Gln Glu Pro Cys Gln Tyr Ser Gln Glu Ser Gln Lys Phe Ser Cys
                165                 170                 175

Gln Leu Ala Val Pro Glu Gly Asp Ser Ser Phe Tyr Ile Val Ser Met
            180                 185                 190

Cys Val Ala Ser Ser Val Gly Ser Lys Phe Ser Lys Thr Gln Thr Phe
        195                 200                 205

Gln Gly Cys Gly Ile Leu Gln Pro Asp Pro Pro Ala Asn Ile Thr Val
    210                 215                 220

Thr Ala Val Ala Arg Asn Pro Arg Trp Leu Ser Val Thr Trp Gln Asp
225                 230                 235                 240

Pro His Ser Trp Asn Ser Ser Phe Tyr Arg Leu Arg Phe Glu Leu Arg
                245                 250                 255

Tyr Arg Ala Glu Arg Ser Lys Thr Phe Thr Thr Trp Met Val Lys Asp
            260                 265                 270

Leu Gln His His Cys Val Ile His Asp Ala Trp Ser Gly Leu Arg His
        275                 280                 285

Val Val Gln Leu Arg Ala Gln Glu Glu Phe Gly Gln Gly Glu Trp Ser
    290                 295                 300

Glu Trp Ser Pro Glu Ala Met Gly Thr Pro Trp Thr Glu Ser Arg Ser
305                 310                 315                 320

Pro Pro Ala Glu Asn Glu Val Ser Thr Pro Met Gln Ala Leu Thr Thr
                325                 330                 335
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```
Asn Lys Asp Asp Asp Asn Ile Leu Phe Arg Asp Ser Ala Asn Ala Thr
            340                 345                 350

Ser Leu Pro Val Gln Asp Ser Ser Ser Val Pro Leu Pro Thr Phe Leu
        355                 360                 365

Val Ala Gly Gly Ser Leu Ala Phe Gly Thr Leu Leu Cys Ile Ala Ile
    370                 375                 380

Val Leu Arg Phe Lys Lys Thr Trp Lys Leu Arg Ala Leu Lys Glu Gly
385                 390                 395                 400

Lys Thr Ser Met His Pro Pro Tyr Ser Leu Gly Gln Leu Val Pro Glu
                405                 410                 415

Arg Pro Arg Pro Thr Pro Val Leu Val Pro Leu Ile Ser Pro Pro Val
            420                 425                 430

Ser Pro Ser Ser Leu Gly Ser Asp Asn Thr Ser Ser His Asn Arg Pro
        435                 440                 445

Asp Ala Arg Asp Pro Arg Ser Pro Tyr Asp Ile Ser Asn Thr Asp Tyr
    450                 455                 460

Phe Phe Pro Arg
465
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<210> 64
<211> 212
<212> PRT
<213> Homo sapiens

<400> 64

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Met Asn Ser Phe Ser Thr Ser Ala Phe Gly Pro Val Ala Phe Ser Leu
1               5                   10                  15

Gly Leu Leu Leu Val Leu Pro Ala Ala Phe Pro Ala Pro Val Pro Pro
            20                  25                  30

Gly Glu Asp Ser Lys Asp Val Ala Ala Pro His Arg Gln Pro Leu Thr
        35                  40                  45
```

Ser Ser Glu Arg Ile Asp Lys Gln Ile Arg Tyr Ile Leu Asp Gly Ile
50 55 60

Ser Ala Leu Arg Lys Glu Thr Cys Asn Lys Ser Asn Met Cys Glu Ser
65 70 75 80

Ser Lys Glu Ala Leu Ala Glu Asn Asn Leu Asn Leu Pro Lys Met Ala
85 90 95

Glu Lys Asp Gly Cys Phe Gln Ser Gly Phe Asn Glu Glu Thr Cys Leu
100 105 110

Val Lys Ile Ile Thr Gly Leu Leu Glu Phe Glu Val Tyr Leu Glu Tyr
115 120 125

Leu Gln Asn Arg Phe Glu Ser Ser Glu Glu Gln Ala Arg Ala Val Gln
130 135 140

Met Ser Thr Lys Val Leu Ile Gln Phe Leu Gln Lys Lys Ala Lys Asn
145 150 155 160

Leu Asp Ala Ile Thr Thr Pro Asp Pro Thr Thr Asn Ala Ser Leu Leu
165 170 175

Thr Lys Leu Gln Ala Gln Asn Gln Trp Leu Gln Asp Met Thr Thr His
180 185 190

Leu Ile Leu Arg Ser Phe Lys Glu Phe Leu Gln Ser Ser Leu Arg Ala
195 200 205

Leu Arg Gln Met
210

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<213> Artificial Sequence

<220>
<223> Linker

<400> 65

Gly Gly Gly Gly Ser
1 5

<210> 66
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<400> 66

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1 5 10

<210> 67
<211> 499
<212> PRT
<213> Artificial Sequence

<220>
<223> IL-6R - IL-6 fusion protein

<400> 67

Leu Ala Pro Arg Arg Cys Pro Ala Gln Glu Val Ala Arg Gly Val Leu
1 5 10 15

Thr Ser Leu Pro Gly Asp Ser Val Thr Leu Thr Cys Pro Gly Val Glu
20 25 30

Pro Glu Asp Asn Ala Thr Val His Trp Val Leu Arg Lys Pro Ala Ala
35 40 45

Gly Ser His Pro Ser Arg Trp Ala Gly Met Gly Arg Arg Leu Leu Leu
50 55 60

Arg Ser Val Gln Leu His Asp Ser Gly Asn Tyr Ser Cys Tyr Arg Ala
65 70 75 80

Gly Arg Pro Ala Gly Thr Val His Leu Leu Val Asp Val Pro Pro Glu
85 90 95

Glu Pro Gln Leu Ser Cys Phe Arg Lys Ser Pro Leu Ser Asn Val Val
100 105 110

```
Cys Glu Trp Gly Pro Arg Ser Thr Pro Ser Leu Thr Thr Lys Ala Val
        115                 120                 125

Leu Leu Val Arg Lys Phe Gln Asn Ser Pro Ala Glu Asp Phe Gln Glu
    130                 135                 140

Pro Cys Gln Tyr Ser Gln Glu Ser Gln Lys Phe Ser Cys Gln Leu Ala
145                 150                 155                 160

Val Pro Glu Gly Asp Ser Ser Phe Tyr Ile Val Ser Met Cys Val Ala
                165                 170                 175

Ser Ser Val Gly Ser Lys Phe Ser Lys Thr Gln Thr Phe Gln Gly Cys
            180                 185                 190

Gly Ile Leu Gln Pro Asp Pro Pro Ala Asn Ile Thr Val Thr Ala Val
        195                 200                 205

Ala Arg Asn Pro Arg Trp Leu Ser Val Thr Trp Gln Asp Pro His Ser
    210                 215                 220

Trp Asn Ser Ser Phe Tyr Arg Leu Arg Phe Glu Leu Arg Tyr Arg Ala
225                 230                 235                 240

Glu Arg Ser Lys Thr Phe Thr Thr Trp Met Val Lys Asp Leu Gln His
                245                 250                 255

His Cys Val Ile His Asp Ala Trp Ser Gly Leu Arg His Val Val Gln
            260                 265                 270

Leu Arg Ala Gln Glu Glu Phe Gly Gln Gly Glu Trp Ser Glu Trp Ser
        275                 280                 285

Pro Glu Ala Met Gly Thr Pro Trp Thr Glu Ser Arg Ser Pro Pro Ala
    290                 295                 300

Glu Asn Glu Val Ser Thr Pro Met Gln Ala Ala Pro Val Pro Pro Gly
305                 310                 315                 320

Glu Asp Ser Lys Asp Val Ala Ala Pro His Arg Gln Pro Leu Thr Ser
                325                 330                 335
```

```
Ser Glu Arg Ile Asp Lys Gln Ile Arg Tyr Ile Leu Asp Gly Ile Ser
            340                 345                 350

Ala Leu Arg Lys Glu Thr Cys Asn Lys Ser Asn Met Cys Glu Ser Ser
        355                 360                 365

Lys Glu Ala Leu Ala Glu Asn Asn Leu Asn Leu Pro Lys Met Ala Glu
    370                 375                 380

Lys Asp Gly Cys Phe Gln Ser Gly Phe Asn Glu Glu Thr Cys Leu Val
385                 390                 395                 400

Lys Ile Ile Thr Gly Leu Leu Glu Phe Glu Val Tyr Leu Glu Tyr Leu
                405                 410                 415

Gln Asn Arg Phe Glu Ser Ser Glu Glu Gln Ala Arg Ala Val Gln Met
            420                 425                 430

Ser Thr Lys Val Leu Ile Gln Phe Leu Gln Lys Lys Ala Lys Asn Leu
        435                 440                 445

Asp Ala Ile Thr Thr Pro Asp Pro Thr Thr Asn Ala Ser Leu Leu Thr
    450                 455                 460

Lys Leu Gln Ala Gln Asn Gln Trp Leu Gln Asp Met Thr Thr His Leu
465                 470                 475                 480

Ile Leu Arg Ser Phe Lys Glu Phe Leu Gln Ser Ser Leu Arg Ala Leu
                485                 490                 495

Arg Gln Met
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<210> 68
<211> 489
<212> PRT
<213> Artificial Sequence

<220>
<223> IL-6R - IL-6 fusion protein

<400> 68

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1               5                  10                  15

Thr Ser Leu Pro Gly Asp Ser Val Thr Leu Thr Cys Pro Gly Val Glu
            20                  25                  30

Pro Glu Asp Asn Ala Thr Val His Trp Val Leu Arg Lys Pro Ala Ala
        35                  40                  45

Gly Ser His Pro Ser Arg Trp Ala Gly Met Gly Arg Arg Leu Leu Leu
    50                  55                  60

Arg Ser Val Gln Leu His Asp Ser Gly Asn Tyr Ser Cys Tyr Arg Ala
65                  70                  75                  80

Gly Arg Pro Ala Gly Thr Val His Leu Leu Val Asp Val Pro Pro Glu
                85                  90                  95

Glu Pro Gln Leu Ser Cys Phe Arg Lys Ser Pro Leu Ser Asn Val Val
            100                 105                 110

Cys Glu Trp Gly Pro Arg Ser Thr Pro Ser Leu Thr Thr Lys Ala Val
        115                 120                 125

Leu Leu Val Arg Lys Phe Gln Asn Ser Pro Ala Glu Asp Phe Gln Glu
    130                 135                 140

Pro Cys Gln Tyr Ser Gln Glu Ser Gln Lys Phe Ser Cys Gln Leu Ala
145                 150                 155                 160

Val Pro Glu Gly Asp Ser Ser Phe Tyr Ile Val Ser Met Cys Val Ala
                165                 170                 175

Ser Ser Val Gly Ser Lys Phe Ser Lys Thr Gln Thr Phe Gln Gly Cys
            180                 185                 190

Gly Ile Leu Gln Pro Asp Pro Pro Ala Asn Ile Thr Val Thr Ala Val
        195                 200                 205

Ala Arg Asn Pro Arg Trp Leu Ser Val Thr Trp Gln Asp Pro His Ser
    210                 215                 220
```

```
Trp Asn Ser Ser Phe Tyr Arg Leu Arg Phe Glu Leu Arg Tyr Arg Ala
225                 230                 235                 240

Glu Arg Ser Lys Thr Phe Thr Thr Trp Met Val Lys Asp Leu Gln His
                245                 250                 255

His Cys Val Ile His Asp Ala Trp Ser Gly Leu Arg His Val Val Gln
            260                 265                 270

Leu Arg Ala Gln Glu Glu Phe Gly Gln Gly Glu Trp Ser Glu Trp Ser
        275                 280                 285

Pro Glu Ala Met Gly Thr Pro Trp Thr Glu Ser Arg Ser Pro Pro Ala
    290                 295                 300

Ala Pro Val Pro Pro Gly Glu Asp Ser Lys Asp Val Ala Ala Pro His
305                 310                 315                 320

Arg Gln Pro Leu Thr Ser Ser Glu Arg Ile Asp Lys Gln Ile Arg Tyr
                325                 330                 335

Ile Leu Asp Gly Ile Ser Ala Leu Arg Lys Glu Thr Cys Asn Lys Ser
            340                 345                 350

Asn Met Cys Glu Ser Ser Lys Glu Ala Leu Ala Glu Asn Asn Leu Asn
        355                 360                 365

Leu Pro Lys Met Ala Glu Lys Asp Gly Cys Phe Gln Ser Gly Phe Asn
    370                 375                 380

Glu Glu Thr Cys Leu Val Lys Ile Ile Thr Gly Leu Leu Glu Phe Glu
385                 390                 395                 400

Val Tyr Leu Glu Tyr Leu Gln Asn Arg Phe Glu Ser Ser Glu Glu Gln
                405                 410                 415

Ala Arg Ala Val Gln Met Ser Thr Lys Val Leu Ile Gln Phe Leu Gln
            420                 425                 430

Lys Lys Ala Lys Asn Leu Asp Ala Ile Thr Thr Pro Asp Pro Thr Thr
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435 440 445

Asn Ala Ser Leu Leu Thr Lys Leu Gln Ala Gln Asn Gln Trp Leu Gln
450 455 460

Asp Met Thr Thr His Leu Ile Leu Arg Ser Phe Lys Glu Phe Leu Gln
465 470 475 480

Ser Ser Leu Arg Ala Leu Arg Gln Met
485

<210> 69
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<400> 69

Gly Gly Gly Gly
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<210> 70
<211> 527
<212> PRT
<213> Artificial Sequence

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<223> IL-6R - IL-6 fusion protein

<400> 70

Leu Ala Pro Arg Arg Cys Pro Ala Gln Glu Val Ala Arg Gly Val Leu
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Thr Ser Leu Pro Gly Asp Ser Val Thr Leu Thr Cys Pro Gly Val Glu
20 25 30

Pro Glu Asp Asn Ala Thr Val His Trp Val Leu Arg Lys Pro Ala Ala
35 40 45

Gly Ser His Pro Ser Arg Trp Ala Gly Met Gly Arg Arg Leu Leu Leu
50 55 60

```
Arg Ser Val Gln Leu His Asp Ser Gly Asn Tyr Ser Cys Tyr Arg Ala
65                  70                  75                  80

Gly Arg Pro Ala Gly Thr Val His Leu Leu Val Asp Val Pro Pro Glu
                85                  90                  95

Glu Pro Gln Leu Ser Cys Phe Arg Lys Ser Pro Leu Ser Asn Val Val
            100                 105                 110

Cys Glu Trp Gly Pro Arg Ser Thr Pro Ser Leu Thr Thr Lys Ala Val
        115                 120                 125

Leu Leu Val Arg Lys Phe Gln Asn Ser Pro Ala Glu Asp Phe Gln Glu
    130                 135                 140

Pro Cys Gln Tyr Ser Gln Glu Ser Gln Lys Phe Ser Cys Gln Leu Ala
145                 150                 155                 160

Val Pro Glu Gly Asp Ser Ser Phe Tyr Ile Val Ser Met Cys Val Ala
                165                 170                 175

Ser Ser Val Gly Ser Lys Phe Ser Lys Thr Gln Thr Phe Gln Gly Cys
            180                 185                 190

Gly Ile Leu Gln Pro Asp Pro Pro Ala Asn Ile Thr Val Thr Ala Val
        195                 200                 205

Ala Arg Asn Pro Arg Trp Leu Ser Val Thr Trp Gln Asp Pro His Ser
    210                 215                 220

Trp Asn Ser Ser Phe Tyr Arg Leu Arg Phe Glu Leu Arg Tyr Arg Ala
225                 230                 235                 240

Glu Arg Ser Lys Thr Phe Thr Thr Trp Met Val Lys Asp Leu Gln His
                245                 250                 255

His Cys Val Ile His Asp Ala Trp Ser Gly Leu Arg His Val Val Gln
            260                 265                 270

Leu Arg Ala Gln Glu Glu Phe Gly Gln Gly Glu Trp Ser Glu Trp Ser
        275                 280                 285
```

```
Pro Glu Ala Met Gly Thr Pro Trp Thr Glu Ser Arg Ser Pro Pro Ala
    290                 295                 300

Glu Asn Glu Val Ser Thr Pro Met Gln Ala Leu Thr Thr Asn Lys Asp
305                 310                 315                 320

Asp Asp Asn Ile Leu Phe Arg Asp Ser Ala Asn Ala Thr Ser Leu Pro
                325                 330                 335

Val Gln Asp Ser Ser Ser Ala Pro Val Pro Pro Gly Glu Asp Ser Lys
            340                 345                 350

Asp Val Ala Ala Pro His Arg Gln Pro Leu Thr Ser Ser Glu Arg Ile
        355                 360                 365

Asp Lys Gln Ile Arg Tyr Ile Leu Asp Gly Ile Ser Ala Leu Arg Lys
    370                 375                 380

Glu Thr Cys Asn Lys Ser Asn Met Cys Glu Ser Ser Lys Glu Ala Leu
385                 390                 395                 400

Ala Glu Asn Asn Leu Asn Leu Pro Lys Met Ala Glu Lys Asp Gly Cys
                405                 410                 415

Phe Gln Ser Gly Phe Asn Glu Glu Thr Cys Leu Val Lys Ile Ile Thr
            420                 425                 430

Gly Leu Leu Glu Phe Glu Val Tyr Leu Glu Tyr Leu Gln Asn Arg Phe
        435                 440                 445

Glu Ser Ser Glu Glu Gln Ala Arg Ala Val Gln Met Ser Thr Lys Val
    450                 455                 460

Leu Ile Gln Phe Leu Gln Lys Lys Ala Lys Asn Leu Asp Ala Ile Thr
465                 470                 475                 480

Thr Pro Asp Pro Thr Thr Asn Ala Ser Leu Leu Thr Lys Leu Gln Ala
                485                 490                 495

Gln Asn Gln Trp Leu Gln Asp Met Thr Thr His Leu Ile Leu Arg Ser
            500                 505                 510
```

Phe Lys Glu Phe Leu Gln Ser Ser Leu Arg Ala Leu Arg Gln Met
515 520 525

<210> 71
<211> 524
<212> PRT
<213> Artificial Sequence

<220>
<223> IL-6R - IL-6 fusion protein

<400> 71

Leu Ala Pro Arg Arg Cys Pro Ala Gln Glu Val Ala Arg Gly Val Leu
1 5 10 15

Thr Ser Leu Pro Gly Asp Ser Val Thr Leu Thr Cys Pro Gly Val Glu
20 25 30

Pro Glu Asp Asn Ala Thr Val His Trp Val Leu Arg Lys Pro Ala Ala
35 40 45

Gly Ser His Pro Ser Arg Trp Ala Gly Met Gly Arg Arg Leu Leu Leu
50 55 60

Arg Ser Val Gln Leu His Asp Ser Gly Asn Tyr Ser Cys Tyr Arg Ala
65 70 75 80

Gly Arg Pro Ala Gly Thr Val His Leu Leu Val Asp Val Pro Pro Glu
85 90 95

Glu Pro Gln Leu Ser Cys Phe Arg Lys Ser Pro Leu Ser Asn Val Val
100 105 110

Cys Glu Trp Gly Pro Arg Ser Thr Pro Ser Leu Thr Thr Lys Ala Val
115 120 125

Leu Leu Val Arg Lys Phe Gln Asn Ser Pro Ala Glu Asp Phe Gln Glu
130 135 140

Pro Cys Gln Tyr Ser Gln Glu Ser Gln Lys Phe Ser Cys Gln Leu Ala
145 150 155 160

```
Val Pro Glu Gly Asp Ser Ser Phe Tyr Ile Val Ser Met Cys Val Ala
                 165                 170                 175

Ser Ser Val Gly Ser Lys Phe Ser Lys Thr Gln Thr Phe Gln Gly Cys
            180                 185                 190

Gly Ile Leu Gln Pro Asp Pro Pro Ala Asn Ile Thr Val Thr Ala Val
        195                 200                 205

Ala Arg Asn Pro Arg Trp Leu Ser Val Thr Trp Gln Asp Pro His Ser
    210                 215                 220

Trp Asn Ser Ser Phe Tyr Arg Leu Arg Phe Glu Leu Arg Tyr Arg Ala
225                 230                 235                 240

Glu Arg Ser Lys Thr Phe Thr Thr Trp Met Val Lys Asp Leu Gln His
                245                 250                 255

His Cys Val Ile His Asp Ala Trp Ser Gly Leu Arg His Val Val Gln
            260                 265                 270

Leu Arg Ala Gln Glu Glu Phe Gly Gln Gly Glu Trp Ser Glu Trp Ser
        275                 280                 285

Pro Glu Ala Met Gly Thr Pro Trp Thr Glu Ser Arg Ser Pro Pro Ala
    290                 295                 300

Glu Asn Glu Val Ser Thr Pro Met Gln Ala Leu Thr Thr Asn Lys Asp
305                 310                 315                 320

Asp Asp Asn Ile Leu Phe Arg Asp Ser Ala Asn Ala Thr Ser Leu Pro
                325                 330                 335

Val Gln Asp Ala Pro Val Pro Pro Gly Glu Asp Ser Lys Asp Val Ala
            340                 345                 350

Ala Pro His Arg Gln Pro Leu Thr Ser Ser Glu Arg Ile Asp Lys Gln
        355                 360                 365

Ile Arg Tyr Ile Leu Asp Gly Ile Ser Ala Leu Arg Lys Glu Thr Cys
    370                 375                 380
```

```
Asn Lys Ser Asn Met Cys Glu Ser Ser Lys Glu Ala Leu Ala Glu Asn
385                 390                 395                 400

Asn Leu Asn Leu Pro Lys Met Ala Glu Lys Asp Gly Cys Phe Gln Ser
                405                 410                 415

Gly Phe Asn Glu Glu Thr Cys Leu Val Lys Ile Ile Thr Gly Leu Leu
            420                 425                 430

Glu Phe Glu Val Tyr Leu Glu Tyr Leu Gln Asn Arg Phe Glu Ser Ser
        435                 440                 445

Glu Glu Gln Ala Arg Ala Val Gln Met Ser Thr Lys Val Leu Ile Gln
    450                 455                 460

Phe Leu Gln Lys Lys Ala Lys Asn Leu Asp Ala Ile Thr Thr Pro Asp
465                 470                 475                 480

Pro Thr Thr Asn Ala Ser Leu Leu Thr Lys Leu Gln Ala Gln Asn Gln
                485                 490                 495

Trp Leu Gln Asp Met Thr Thr His Leu Ile Leu Arg Ser Phe Lys Glu
            500                 505                 510

Phe Leu Gln Ser Ser Leu Arg Ala Leu Arg Gln Met
        515                 520
```

<210> 72
<211> 518
<212> PRT
<213> Artificial Sequence

<220>
<223> IL-6R - IL-6 fusion protein

<400> 72

```
Leu Ala Pro Arg Arg Cys Pro Ala Gln Glu Val Ala Arg Gly Val Leu
1               5                   10                  15

Thr Ser Leu Pro Gly Asp Ser Val Thr Leu Thr Cys Pro Gly Val Glu
            20                  25                  30
```

```
Pro Glu Asp Asn Ala Thr Val His Trp Val Leu Arg Lys Pro Ala Ala
        35                  40                  45

Gly Ser His Pro Ser Arg Trp Ala Gly Met Gly Arg Arg Leu Leu Leu
    50                  55                  60

Arg Ser Val Gln Leu His Asp Ser Gly Asn Tyr Ser Cys Tyr Arg Ala
65                  70                  75                  80

Gly Arg Pro Ala Gly Thr Val His Leu Leu Val Asp Val Pro Pro Glu
                85                  90                  95

Glu Pro Gln Leu Ser Cys Phe Arg Lys Ser Pro Leu Ser Asn Val Val
            100                 105                 110

Cys Glu Trp Gly Pro Arg Ser Thr Pro Ser Leu Thr Thr Lys Ala Val
        115                 120                 125

Leu Leu Val Arg Lys Phe Gln Asn Ser Pro Ala Glu Asp Phe Gln Glu
    130                 135                 140

Pro Cys Gln Tyr Ser Gln Glu Ser Gln Lys Phe Ser Cys Gln Leu Ala
145                 150                 155                 160

Val Pro Glu Gly Asp Ser Ser Phe Tyr Ile Val Ser Met Cys Val Ala
                165                 170                 175

Ser Ser Val Gly Ser Lys Phe Ser Lys Thr Gln Thr Phe Gln Gly Cys
            180                 185                 190

Gly Ile Leu Gln Pro Asp Pro Pro Ala Asn Ile Thr Val Thr Ala Val
        195                 200                 205

Ala Arg Asn Pro Arg Trp Leu Ser Val Thr Trp Gln Asp Pro His Ser
    210                 215                 220

Trp Asn Ser Ser Phe Tyr Arg Leu Arg Phe Glu Leu Arg Tyr Arg Ala
225                 230                 235                 240

Glu Arg Ser Lys Thr Phe Thr Thr Trp Met Val Lys Asp Leu Gln His
                245                 250                 255
```

```
His Cys Val Ile His Asp Ala Trp Ser Gly Leu Arg His Val Val Gln
            260                 265                 270

Leu Arg Ala Gln Glu Glu Phe Gly Gln Gly Glu Trp Ser Glu Trp Ser
        275                 280                 285

Pro Glu Ala Met Gly Thr Pro Trp Thr Glu Ser Arg Ser Pro Pro Ala
    290                 295                 300

Glu Asn Glu Val Ser Thr Pro Met Gln Ala Leu Thr Thr Asn Lys Asp
305                 310                 315                 320

Asp Asp Asn Ile Leu Phe Arg Asp Ser Ala Asn Ala Thr Ala Pro Val
                325                 330                 335

Pro Pro Gly Glu Asp Ser Lys Asp Val Ala Ala Pro His Arg Gln Pro
            340                 345                 350

Leu Thr Ser Ser Glu Arg Ile Asp Lys Gln Ile Arg Tyr Ile Leu Asp
        355                 360                 365

Gly Ile Ser Ala Leu Arg Lys Glu Thr Cys Asn Lys Ser Asn Met Cys
    370                 375                 380

Glu Ser Ser Lys Glu Ala Leu Ala Glu Asn Asn Leu Asn Leu Pro Lys
385                 390                 395                 400

Met Ala Glu Lys Asp Gly Cys Phe Gln Ser Gly Phe Asn Glu Glu Thr
                405                 410                 415

Cys Leu Val Lys Ile Ile Thr Gly Leu Leu Glu Phe Glu Val Tyr Leu
            420                 425                 430

Glu Tyr Leu Gln Asn Arg Phe Glu Ser Ser Glu Glu Gln Ala Arg Ala
        435                 440                 445

Val Gln Met Ser Thr Lys Val Leu Ile Gln Phe Leu Gln Lys Lys Ala
    450                 455                 460

Lys Asn Leu Asp Ala Ile Thr Thr Pro Asp Pro Thr Thr Asn Ala Ser
```

465 470 475 480

Leu Leu Thr Lys Leu Gln Ala Gln Asn Gln Trp Leu Gln Asp Met Thr
485 490 495

Thr His Leu Ile Leu Arg Ser Phe Lys Glu Phe Leu Gln Ser Ser Leu
500 505 510

Arg Ala Leu Arg Gln Met
515

<210> 73
<211> 512
<212> PRT
<213> Artificial Sequence

<220>
<223> IL-6R - IL-6 fusion protein

<400> 73

Leu Ala Pro Arg Arg Cys Pro Ala Gln Glu Val Ala Arg Gly Val Leu
1 5 10 15

Thr Ser Leu Pro Gly Asp Ser Val Thr Leu Thr Cys Pro Gly Val Glu
20 25 30

Pro Glu Asp Asn Ala Thr Val His Trp Val Leu Arg Lys Pro Ala Ala
35 40 45

Gly Ser His Pro Ser Arg Trp Ala Gly Met Gly Arg Arg Leu Leu Leu
50 55 60

Arg Ser Val Gln Leu His Asp Ser Gly Asn Tyr Ser Cys Tyr Arg Ala
65 70 75 80

Gly Arg Pro Ala Gly Thr Val His Leu Leu Val Asp Val Pro Pro Glu
85 90 95

Glu Pro Gln Leu Ser Cys Phe Arg Lys Ser Pro Leu Ser Asn Val Val
100 105 110

Cys Glu Trp Gly Pro Arg Ser Thr Pro Ser Leu Thr Thr Lys Ala Val
115 120 125

```
Leu Leu Val Arg Lys Phe Gln Asn Ser Pro Ala Glu Asp Phe Gln Glu
    130                 135                 140

Pro Cys Gln Tyr Ser Gln Glu Ser Gln Lys Phe Ser Cys Gln Leu Ala
145                 150                 155                 160

Val Pro Glu Gly Asp Ser Ser Phe Tyr Ile Val Ser Met Cys Val Ala
                165                 170                 175

Ser Ser Val Gly Ser Lys Phe Ser Lys Thr Gln Thr Phe Gln Gly Cys
            180                 185                 190

Gly Ile Leu Gln Pro Asp Pro Pro Ala Asn Ile Thr Val Thr Ala Val
        195                 200                 205

Ala Arg Asn Pro Arg Trp Leu Ser Val Thr Trp Gln Asp Pro His Ser
    210                 215                 220

Trp Asn Ser Ser Phe Tyr Arg Leu Arg Phe Glu Leu Arg Tyr Arg Ala
225                 230                 235                 240

Glu Arg Ser Lys Thr Phe Thr Thr Trp Met Val Lys Asp Leu Gln His
                245                 250                 255

His Cys Val Ile His Asp Ala Trp Ser Gly Leu Arg His Val Val Gln
            260                 265                 270

Leu Arg Ala Gln Glu Glu Phe Gly Gln Gly Glu Trp Ser Glu Trp Ser
        275                 280                 285

Pro Glu Ala Met Gly Thr Pro Trp Thr Glu Ser Arg Ser Pro Pro Ala
    290                 295                 300

Glu Asn Glu Val Ser Thr Pro Met Gln Ala Leu Thr Thr Asn Lys Asp
305                 310                 315                 320

Asp Asp Asn Ile Leu Phe Arg Ala Pro Val Pro Pro Gly Glu Asp Ser
                325                 330                 335

Lys Asp Val Ala Ala Pro His Arg Gln Pro Leu Thr Ser Ser Glu Arg
```

340 345 350

Ile Asp Lys Gln Ile Arg Tyr Ile Leu Asp Gly Ile Ser Ala Leu Arg
355 360 365

Lys Glu Thr Cys Asn Lys Ser Asn Met Cys Glu Ser Ser Lys Glu Ala
370 375 380

Leu Ala Glu Asn Asn Leu Asn Leu Pro Lys Met Ala Glu Lys Asp Gly
385 390 395 400

Cys Phe Gln Ser Gly Phe Asn Glu Glu Thr Cys Leu Val Lys Ile Ile
405 410 415

Thr Gly Leu Leu Glu Phe Glu Val Tyr Leu Glu Tyr Leu Gln Asn Arg
420 425 430

Phe Glu Ser Ser Glu Glu Gln Ala Arg Ala Val Gln Met Ser Thr Lys
435 440 445

Val Leu Ile Gln Phe Leu Gln Lys Lys Ala Lys Asn Leu Asp Ala Ile
450 455 460

Thr Thr Pro Asp Pro Thr Thr Asn Ala Ser Leu Leu Thr Lys Leu Gln
465 470 475 480

Ala Gln Asn Gln Trp Leu Gln Asp Met Thr Thr His Leu Ile Leu Arg
485 490 495

Ser Phe Lys Glu Phe Leu Gln Ser Ser Leu Arg Ala Leu Arg Gln Met
500 505 510

<210> 74
<211> 509
<212> PRT
<213> Artificial Sequence

<220>
<223> IL-6R - IL-6 fusion protein

<400> 74

Leu Ala Pro Arg Arg Cys Pro Ala Gln Glu Val Ala Arg Gly Val Leu
1 5 10 15

```
Thr Ser Leu Pro Gly Asp Ser Val Thr Leu Thr Cys Pro Gly Val Glu
            20                  25                  30

Pro Glu Asp Asn Ala Thr Val His Trp Val Leu Arg Lys Pro Ala Ala
        35                  40                  45

Gly Ser His Pro Ser Arg Trp Ala Gly Met Gly Arg Arg Leu Leu Leu
    50                  55                  60

Arg Ser Val Gln Leu His Asp Ser Gly Asn Tyr Ser Cys Tyr Arg Ala
65                  70                  75                  80

Gly Arg Pro Ala Gly Thr Val His Leu Leu Val Asp Val Pro Pro Glu
                85                  90                  95

Glu Pro Gln Leu Ser Cys Phe Arg Lys Ser Pro Leu Ser Asn Val Val
            100                 105                 110

Cys Glu Trp Gly Pro Arg Ser Thr Pro Ser Leu Thr Thr Lys Ala Val
        115                 120                 125

Leu Leu Val Arg Lys Phe Gln Asn Ser Pro Ala Glu Asp Phe Gln Glu
    130                 135                 140

Pro Cys Gln Tyr Ser Gln Glu Ser Gln Lys Phe Ser Cys Gln Leu Ala
145                 150                 155                 160

Val Pro Glu Gly Asp Ser Ser Phe Tyr Ile Val Ser Met Cys Val Ala
                165                 170                 175

Ser Ser Val Gly Ser Lys Phe Ser Lys Thr Gln Thr Phe Gln Gly Cys
            180                 185                 190

Gly Ile Leu Gln Pro Asp Pro Pro Ala Asn Ile Thr Val Thr Ala Val
        195                 200                 205

Ala Arg Asn Pro Arg Trp Leu Ser Val Thr Trp Gln Asp Pro His Ser
    210                 215                 220

Trp Asn Ser Ser Phe Tyr Arg Leu Arg Phe Glu Leu Arg Tyr Arg Ala
```

225 230 235 240

Glu Arg Ser Lys Thr Phe Thr Thr Trp Met Val Lys Asp Leu Gln His
245 250 255

His Cys Val Ile His Asp Ala Trp Ser Gly Leu Arg His Val Val Gln
260 265 270

Leu Arg Ala Gln Glu Glu Phe Gly Gln Gly Glu Trp Ser Glu Trp Ser
275 280 285

Pro Glu Ala Met Gly Thr Pro Trp Thr Glu Ser Arg Ser Pro Pro Ala
290 295 300

Glu Asn Glu Val Ser Thr Pro Met Gln Ala Leu Thr Thr Asn Lys Asp
305 310 315 320

Asp Asp Asn Ile Ala Pro Val Pro Pro Gly Glu Asp Ser Lys Asp Val
325 330 335

Ala Ala Pro His Arg Gln Pro Leu Thr Ser Ser Glu Arg Ile Asp Lys
340 345 350

Gln Ile Arg Tyr Ile Leu Asp Gly Ile Ser Ala Leu Arg Lys Glu Thr
355 360 365

Cys Asn Lys Ser Asn Met Cys Glu Ser Ser Lys Glu Ala Leu Ala Glu
370 375 380

Asn Asn Leu Asn Leu Pro Lys Met Ala Glu Lys Asp Gly Cys Phe Gln
385 390 395 400

Ser Gly Phe Asn Glu Glu Thr Cys Leu Val Lys Ile Ile Thr Gly Leu
405 410 415

Leu Glu Phe Glu Val Tyr Leu Glu Tyr Leu Gln Asn Arg Phe Glu Ser
420 425 430

Ser Glu Glu Gln Ala Arg Ala Val Gln Met Ser Thr Lys Val Leu Ile
435 440 445

Gln Phe Leu Gln Lys Lys Ala Lys Asn Leu Asp Ala Ile Thr Thr Pro
450 455 460

Asp Pro Thr Thr Asn Ala Ser Leu Leu Thr Lys Leu Gln Ala Gln Asn
465 470 475 480

Gln Trp Leu Gln Asp Met Thr Thr His Leu Ile Leu Arg Ser Phe Lys
485 490 495

Glu Phe Leu Gln Ser Ser Leu Arg Ala Leu Arg Gln Met
500 505

<210> 75
<211> 504
<212> PRT
<213> Artificial Sequence

<220>
<223> IL-6R - IL-6 fusion protein

<400> 75

Leu Ala Pro Arg Arg Cys Pro Ala Gln Glu Val Ala Arg Gly Val Leu
1 5 10 15

Thr Ser Leu Pro Gly Asp Ser Val Thr Leu Thr Cys Pro Gly Val Glu
20 25 30

Pro Glu Asp Asn Ala Thr Val His Trp Val Leu Arg Lys Pro Ala Ala
35 40 45

Gly Ser His Pro Ser Arg Trp Ala Gly Met Gly Arg Arg Leu Leu Leu
50 55 60

Arg Ser Val Gln Leu His Asp Ser Gly Asn Tyr Ser Cys Tyr Arg Ala
65 70 75 80

Gly Arg Pro Ala Gly Thr Val His Leu Leu Val Asp Val Pro Pro Glu
85 90 95

Glu Pro Gln Leu Ser Cys Phe Arg Lys Ser Pro Leu Ser Asn Val Val
100 105 110

Cys Glu Trp Gly Pro Arg Ser Thr Pro Ser Leu Thr Thr Lys Ala Val

```
        115                 120                 125

Leu Leu Val Arg Lys Phe Gln Asn Ser Pro Ala Glu Asp Phe Gln Glu
    130                 135                 140

Pro Cys Gln Tyr Ser Gln Glu Ser Gln Lys Phe Ser Cys Gln Leu Ala
145                 150                 155                 160

Val Pro Glu Gly Asp Ser Ser Phe Tyr Ile Val Ser Met Cys Val Ala
                165                 170                 175

Ser Ser Val Gly Ser Lys Phe Ser Lys Thr Gln Thr Phe Gln Gly Cys
            180                 185                 190

Gly Ile Leu Gln Pro Asp Pro Pro Ala Asn Ile Thr Val Thr Ala Val
        195                 200                 205

Ala Arg Asn Pro Arg Trp Leu Ser Val Thr Trp Gln Asp Pro His Ser
    210                 215                 220

Trp Asn Ser Ser Phe Tyr Arg Leu Arg Phe Glu Leu Arg Tyr Arg Ala
225                 230                 235                 240

Glu Arg Ser Lys Thr Phe Thr Thr Trp Met Val Lys Asp Leu Gln His
                245                 250                 255

His Cys Val Ile His Asp Ala Trp Ser Gly Leu Arg His Val Val Gln
            260                 265                 270

Leu Arg Ala Gln Glu Glu Phe Gly Gln Gly Glu Trp Ser Glu Trp Ser
        275                 280                 285

Pro Glu Ala Met Gly Thr Pro Trp Thr Glu Ser Arg Ser Pro Pro Ala
    290                 295                 300

Glu Asn Glu Val Ser Thr Pro Met Gln Ala Leu Thr Thr Asn Lys Ala
305                 310                 315                 320

Pro Val Pro Pro Gly Glu Asp Ser Lys Asp Val Ala Ala Pro His Arg
                325                 330                 335
```

Gln Pro Leu Thr Ser Ser Glu Arg Ile Asp Lys Gln Ile Arg Tyr Ile
340 345 350

Leu Asp Gly Ile Ser Ala Leu Arg Lys Glu Thr Cys Asn Lys Ser Asn
355 360 365

Met Cys Glu Ser Ser Lys Glu Ala Leu Ala Glu Asn Asn Leu Asn Leu
370 375 380

Pro Lys Met Ala Glu Lys Asp Gly Cys Phe Gln Ser Gly Phe Asn Glu
385 390 395 400

Glu Thr Cys Leu Val Lys Ile Ile Thr Gly Leu Leu Glu Phe Glu Val
405 410 415

Tyr Leu Glu Tyr Leu Gln Asn Arg Phe Glu Ser Ser Glu Glu Gln Ala
420 425 430

Arg Ala Val Gln Met Ser Thr Lys Val Leu Ile Gln Phe Leu Gln Lys
435 440 445

Lys Ala Lys Asn Leu Asp Ala Ile Thr Thr Pro Asp Pro Thr Thr Asn
450 455 460

Ala Ser Leu Leu Thr Lys Leu Gln Ala Gln Asn Gln Trp Leu Gln Asp
465 470 475 480

Met Thr Thr His Leu Ile Leu Arg Ser Phe Lys Glu Phe Leu Gln Ser
485 490 495

Ser Leu Arg Ala Leu Arg Gln Met
500

<210> 76
<211> 501
<212> PRT
<213> Artificial Sequence

<220>
<223> IL-6R - IL-6 fusion protein

<400> 76

Leu Ala Pro Arg Arg Cys Pro Ala Gln Glu Val Ala Arg Gly Val Leu

1 5 10 15

Thr Ser Leu Pro Gly Asp Ser Val Thr Leu Thr Cys Pro Gly Val Glu
20 25 30

Pro Glu Asp Asn Ala Thr Val His Trp Val Leu Arg Lys Pro Ala Ala
35 40 45

Gly Ser His Pro Ser Arg Trp Ala Gly Met Gly Arg Arg Leu Leu Leu
50 55 60

Arg Ser Val Gln Leu His Asp Ser Gly Asn Tyr Ser Cys Tyr Arg Ala
65 70 75 80

Gly Arg Pro Ala Gly Thr Val His Leu Leu Val Asp Val Pro Pro Glu
85 90 95

Glu Pro Gln Leu Ser Cys Phe Arg Lys Ser Pro Leu Ser Asn Val Val
100 105 110

Cys Glu Trp Gly Pro Arg Ser Thr Pro Ser Leu Thr Thr Lys Ala Val
115 120 125

Leu Leu Val Arg Lys Phe Gln Asn Ser Pro Ala Glu Asp Phe Gln Glu
130 135 140

Pro Cys Gln Tyr Ser Gln Glu Ser Gln Lys Phe Ser Cys Gln Leu Ala
145 150 155 160

Val Pro Glu Gly Asp Ser Ser Phe Tyr Ile Val Ser Met Cys Val Ala
165 170 175

Ser Ser Val Gly Ser Lys Phe Ser Lys Thr Gln Thr Phe Gln Gly Cys
180 185 190

Gly Ile Leu Gln Pro Asp Pro Pro Ala Asn Ile Thr Val Thr Ala Val
195 200 205

Ala Arg Asn Pro Arg Trp Leu Ser Val Thr Trp Gln Asp Pro His Ser
210 215 220

```
Trp Asn Ser Ser Phe Tyr Arg Leu Arg Phe Glu Leu Arg Tyr Arg Ala
225                 230                 235                 240

Glu Arg Ser Lys Thr Phe Thr Thr Trp Met Val Lys Asp Leu Gln His
                245                 250                 255

His Cys Val Ile His Asp Ala Trp Ser Gly Leu Arg His Val Val Gln
            260                 265                 270

Leu Arg Ala Gln Glu Glu Phe Gly Gln Gly Glu Trp Ser Glu Trp Ser
        275                 280                 285

Pro Glu Ala Met Gly Thr Pro Trp Thr Glu Ser Arg Ser Pro Pro Ala
    290                 295                 300

Glu Asn Glu Val Ser Thr Pro Met Gln Ala Leu Thr Ala Pro Val Pro
305                 310                 315                 320

Pro Gly Glu Asp Ser Lys Asp Val Ala Ala Pro His Arg Gln Pro Leu
                325                 330                 335

Thr Ser Ser Glu Arg Ile Asp Lys Gln Ile Arg Tyr Ile Leu Asp Gly
            340                 345                 350

Ile Ser Ala Leu Arg Lys Glu Thr Cys Asn Lys Ser Asn Met Cys Glu
        355                 360                 365

Ser Ser Lys Glu Ala Leu Ala Glu Asn Asn Leu Asn Leu Pro Lys Met
    370                 375                 380

Ala Glu Lys Asp Gly Cys Phe Gln Ser Gly Phe Asn Glu Glu Thr Cys
385                 390                 395                 400

Leu Val Lys Ile Ile Thr Gly Leu Leu Glu Phe Glu Val Tyr Leu Glu
                405                 410                 415

Tyr Leu Gln Asn Arg Phe Glu Ser Ser Glu Glu Gln Ala Arg Ala Val
            420                 425                 430

Gln Met Ser Thr Lys Val Leu Ile Gln Phe Leu Gln Lys Lys Ala Lys
        435                 440                 445
```

Asn Leu Asp Ala Ile Thr Thr Pro Asp Pro Thr Thr Asn Ala Ser Leu
450 455 460

Leu Thr Lys Leu Gln Ala Gln Asn Gln Trp Leu Gln Asp Met Thr Thr
465 470 475 480

His Leu Ile Leu Arg Ser Phe Lys Glu Phe Leu Gln Ser Ser Leu Arg
485 490 495

Ala Leu Arg Gln Met
500

<210> 77
<211> 508
<212> PRT
<213> Artificial Sequence

<220>
<223> IL-6R - IL-6 fusion protein

<400> 77

Leu Ala Pro Arg Arg Cys Pro Ala Gln Glu Val Ala Arg Gly Val Leu
1 5 10 15

Thr Ser Leu Pro Gly Asp Ser Val Thr Leu Thr Cys Pro Gly Val Glu
20 25 30

Pro Glu Asp Asn Ala Thr Val His Trp Val Leu Arg Lys Pro Ala Ala
35 40 45

Gly Ser His Pro Ser Arg Trp Ala Gly Met Gly Arg Arg Leu Leu Leu
50 55 60

Arg Ser Val Gln Leu His Asp Ser Gly Asn Tyr Ser Cys Tyr Arg Ala
65 70 75 80

Gly Arg Pro Ala Gly Thr Val His Leu Leu Val Asp Val Pro Pro Glu
85 90 95

Glu Pro Gln Leu Ser Cys Phe Arg Lys Ser Pro Leu Ser Asn Val Val
100 105 110

```
Cys Glu Trp Gly Pro Arg Ser Thr Pro Ser Leu Thr Thr Lys Ala Val
        115                 120                 125

Leu Leu Val Arg Lys Phe Gln Asn Ser Pro Ala Glu Asp Phe Gln Glu
    130                 135                 140

Pro Cys Gln Tyr Ser Gln Glu Ser Gln Lys Phe Ser Cys Gln Leu Ala
145                 150                 155                 160

Val Pro Glu Gly Asp Ser Ser Phe Tyr Ile Val Ser Met Cys Val Ala
                165                 170                 175

Ser Ser Val Gly Ser Lys Phe Ser Lys Thr Gln Thr Phe Gln Gly Cys
            180                 185                 190

Gly Ile Leu Gln Pro Asp Pro Pro Ala Asn Ile Thr Val Thr Ala Val
        195                 200                 205

Ala Arg Asn Pro Arg Trp Leu Ser Val Thr Trp Gln Asp Pro His Ser
    210                 215                 220

Trp Asn Ser Ser Phe Tyr Arg Leu Arg Phe Glu Leu Arg Tyr Arg Ala
225                 230                 235                 240

Glu Arg Ser Lys Thr Phe Thr Thr Trp Met Val Lys Asp Leu Gln His
                245                 250                 255

His Cys Val Ile His Asp Ala Trp Ser Gly Leu Arg His Val Val Gln
            260                 265                 270

Leu Arg Ala Gln Glu Glu Phe Gly Gln Gly Glu Trp Ser Glu Trp Ser
        275                 280                 285

Pro Glu Ala Met Gly Thr Pro Trp Thr Glu Ser Arg Ser Pro Pro Ala
    290                 295                 300

Glu Asn Glu Val Ser Thr Pro Met Gln Ala Leu Thr Thr Asn Lys Asp
305                 310                 315                 320

Asp Asp Asn Ile Pro Val Pro Pro Gly Glu Asp Ser Lys Asp Val Ala
                325                 330                 335
```

Ala Pro His Arg Gln Pro Leu Thr Ser Ser Glu Arg Ile Asp Lys Gln
340 345 350

Ile Arg Tyr Ile Leu Asp Gly Ile Ser Ala Leu Arg Lys Glu Thr Cys
355 360 365

Asn Lys Ser Asn Met Cys Glu Ser Ser Lys Glu Ala Leu Ala Glu Asn
370 375 380

Asn Leu Asn Leu Pro Lys Met Ala Glu Lys Asp Gly Cys Phe Gln Ser
385 390 395 400

Gly Phe Asn Glu Glu Thr Cys Leu Val Lys Ile Ile Thr Gly Leu Leu
405 410 415

Glu Phe Glu Val Tyr Leu Glu Tyr Leu Gln Asn Arg Phe Glu Ser Ser
420 425 430

Glu Glu Gln Ala Arg Ala Val Gln Met Ser Thr Lys Val Leu Ile Gln
435 440 445

Phe Leu Gln Lys Lys Ala Lys Asn Leu Asp Ala Ile Thr Thr Pro Asp
450 455 460

Pro Thr Thr Asn Ala Ser Leu Leu Thr Lys Leu Gln Ala Gln Asn Gln
465 470 475 480

Trp Leu Gln Asp Met Thr Thr His Leu Ile Leu Arg Ser Phe Lys Glu
485 490 495

Phe Leu Gln Ser Ser Leu Arg Ala Leu Arg Gln Met
500 505

<210> 78
<211> 503
<212> PRT
<213> Artificial Sequence

<220>
<223> IL-6R - IL-6 fusion protein

<400> 78

```
Leu Ala Pro Arg Arg Cys Pro Ala Gln Glu Val Ala Arg Gly Val Leu
1               5                  10                  15

Thr Ser Leu Pro Gly Asp Ser Val Thr Leu Thr Cys Pro Gly Val Glu
            20                  25                  30

Pro Glu Asp Asn Ala Thr Val His Trp Val Leu Arg Lys Pro Ala Ala
        35                  40                  45

Gly Ser His Pro Ser Arg Trp Ala Gly Met Gly Arg Arg Leu Leu Leu
    50                  55                  60

Arg Ser Val Gln Leu His Asp Ser Gly Asn Tyr Ser Cys Tyr Arg Ala
65                  70                  75                  80

Gly Arg Pro Ala Gly Thr Val His Leu Leu Val Asp Val Pro Pro Glu
                85                  90                  95

Glu Pro Gln Leu Ser Cys Phe Arg Lys Ser Pro Leu Ser Asn Val Val
            100                 105                 110

Cys Glu Trp Gly Pro Arg Ser Thr Pro Ser Leu Thr Thr Lys Ala Val
        115                 120                 125

Leu Leu Val Arg Lys Phe Gln Asn Ser Pro Ala Glu Asp Phe Gln Glu
    130                 135                 140

Pro Cys Gln Tyr Ser Gln Glu Ser Gln Lys Phe Ser Cys Gln Leu Ala
145                 150                 155                 160

Val Pro Glu Gly Asp Ser Ser Phe Tyr Ile Val Ser Met Cys Val Ala
                165                 170                 175

Ser Ser Val Gly Ser Lys Phe Ser Lys Thr Gln Thr Phe Gln Gly Cys
            180                 185                 190

Gly Ile Leu Gln Pro Asp Pro Pro Ala Asn Ile Thr Val Thr Ala Val
        195                 200                 205

Ala Arg Asn Pro Arg Trp Leu Ser Val Thr Trp Gln Asp Pro His Ser
    210                 215                 220
```

```
Trp Asn Ser Ser Phe Tyr Arg Leu Arg Phe Glu Leu Arg Tyr Arg Ala
225                 230                 235                 240

Glu Arg Ser Lys Thr Phe Thr Thr Trp Met Val Lys Asp Leu Gln His
                245                 250                 255

His Cys Val Ile His Asp Ala Trp Ser Gly Leu Arg His Val Val Gln
            260                 265                 270

Leu Arg Ala Gln Glu Glu Phe Gly Gln Gly Glu Trp Ser Glu Trp Ser
        275                 280                 285

Pro Glu Ala Met Gly Thr Pro Trp Thr Glu Ser Arg Ser Pro Pro Ala
    290                 295                 300

Glu Asn Glu Val Ser Thr Pro Met Gln Ala Leu Thr Thr Asn Lys Pro
305                 310                 315                 320

Val Pro Pro Gly Glu Asp Ser Lys Asp Val Ala Ala Pro His Arg Gln
                325                 330                 335

Pro Leu Thr Ser Ser Glu Arg Ile Asp Lys Gln Ile Arg Tyr Ile Leu
            340                 345                 350

Asp Gly Ile Ser Ala Leu Arg Lys Glu Thr Cys Asn Lys Ser Asn Met
        355                 360                 365

Cys Glu Ser Ser Lys Glu Ala Leu Ala Glu Asn Asn Leu Asn Leu Pro
    370                 375                 380

Lys Met Ala Glu Lys Asp Gly Cys Phe Gln Ser Gly Phe Asn Glu Glu
385                 390                 395                 400

Thr Cys Leu Val Lys Ile Ile Thr Gly Leu Leu Glu Phe Glu Val Tyr
                405                 410                 415

Leu Glu Tyr Leu Gln Asn Arg Phe Glu Ser Ser Glu Glu Gln Ala Arg
            420                 425                 430

Ala Val Gln Met Ser Thr Lys Val Leu Ile Gln Phe Leu Gln Lys Lys
        435                 440                 445
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Ala Lys Asn Leu Asp Ala Ile Thr Thr Pro Asp Pro Thr Thr Asn Ala
450 455 460

Ser Leu Leu Thr Lys Leu Gln Ala Gln Asn Gln Trp Leu Gln Asp Met
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Thr Thr His Leu Ile Leu Arg Ser Phe Lys Glu Phe Leu Gln Ser Ser
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Leu Arg Ala Leu Arg Gln Met
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Thr Ser Leu Pro Gly Asp Ser Val Thr Leu Thr Cys Pro Gly Val Glu
20 25 30

Pro Glu Asp Asn Ala Thr Val His Trp Val Leu Arg Lys Pro Ala Ala
35 40 45

Gly Ser His Pro Ser Arg Trp Ala Gly Met Gly Arg Arg Leu Leu Leu
50 55 60

Arg Ser Val Gln Leu His Asp Ser Gly Asn Tyr Ser Cys Tyr Arg Ala
65 70 75 80

Gly Arg Pro Ala Gly Thr Val His Leu Leu Val Asp Val Pro Pro Glu
85 90 95

Glu Pro Gln Leu Ser Cys Phe Arg Lys Ser Pro Leu Ser Asn Val Val
100 105 110

Cys Glu Trp Gly Pro Arg Ser Thr Pro Ser Leu Thr Thr Lys Ala Val
115 120 125

Leu Leu Val Arg Lys Phe Gln Asn Ser Pro Ala Glu Asp Phe Gln Glu
130 135 140

Pro Cys Gln Tyr Ser Gln Glu Ser Gln Lys Phe Ser Cys Gln Leu Ala
145 150 155 160

Val Pro Glu Gly Asp Ser Ser Phe Tyr Ile Val Ser Met Cys Val Ala
165 170 175

Ser Ser Val Gly Ser Lys Phe Ser Lys Thr Gln Thr Phe Gln Gly Cys
180 185 190

Gly Ile Leu Gln Pro Asp Pro Pro Ala Asn Ile Thr Val Thr Ala Val
195 200 205

Ala Arg Asn Pro Arg Trp Leu Ser Val Thr Trp Gln Asp Pro His Ser
210 215 220

Trp Asn Ser Ser Phe Tyr Arg Leu Arg Phe Glu Leu Arg Tyr Arg Ala
225 230 235 240

Glu Arg Ser Lys Thr Phe Thr Thr Trp Met Val Lys Asp Leu Gln His
245 250 255

His Cys Val Ile His Asp Ala Trp Ser Gly Leu Arg His Val Val Gln
260 265 270

Leu Arg Ala Gln Glu Glu Phe Gly Gln Gly Glu Trp Ser Glu Trp Ser
275 280 285

Pro Glu Ala Met Gly Thr Pro Trp Thr Glu Ser Arg Ser Pro Pro Ala
290 295 300

Glu Asn Glu Val Ser Thr Pro Met Gln Ala Leu Val Pro Pro Gly Glu
305 310 315 320

Asp Ser Lys Asp Val Ala Ala Pro His Arg Gln Pro Leu Thr Ser Ser
325 330 335

Glu Arg Ile Asp Lys Gln Ile Arg Tyr Ile Leu Asp Gly Ile Ser Ala
340 345 350

Leu Arg Lys Glu Thr Cys Asn Lys Ser Asn Met Cys Glu Ser Ser Lys
355 360 365

Glu Ala Leu Ala Glu Asn Asn Leu Asn Leu Pro Lys Met Ala Glu Lys
370 375 380

Asp Gly Cys Phe Gln Ser Gly Phe Asn Glu Glu Thr Cys Leu Val Lys
385 390 395 400

Ile Ile Thr Gly Leu Leu Glu Phe Glu Val Tyr Leu Glu Tyr Leu Gln
405 410 415

Asn Arg Phe Glu Ser Ser Glu Glu Gln Ala Arg Ala Val Gln Met Ser
420 425 430

Thr Lys Val Leu Ile Gln Phe Leu Gln Lys Lys Ala Lys Asn Leu Asp
435 440 445

Ala Ile Thr Thr Pro Asp Pro Thr Thr Asn Ala Ser Leu Leu Thr Lys
450 455 460

Leu Gln Ala Gln Asn Gln Trp Leu Gln Asp Met Thr Thr His Leu Ile
465 470 475 480

Leu Arg Ser Phe Lys Glu Phe Leu Gln Ser Ser Leu Arg Ala Leu Arg
485 490 495

Gln Met